PATENT COOPERATION TREATY From the INTERNATIONAL SEARCHING AUTHORITY To: DANIEL A. MONACO SEIDEL, GONDA, LAVORGNA, & MONACO, P.C. **SUITE 1800** TWO PENN CENTER PLAZA NOTIFICATION OF TRANSMITTAL OF PHILADELPHIA PA 19102 THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION (PCT Rule 44.1) Date of Mailing 14 FEB 2000 lay/month/year) HACO, P.C Applicant's or agent's file reference FOR FURTHER ACTION See paragraphs 1 and 4 below 6056-279 PC International application No. International filing date (day/month/year) PCT/US99/22756 30 SEPTEMBER 1999 Applicant FRONTICELLI, CLARA The applicant is hereby notified that the international search report has been established and is transmitted herewith. Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46): The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet. Where? Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35 For more detailed instructions, see the notes on the accompanying sheet. The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices. no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made. 4. Further action(s): The applicant is reminded of the following: Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication. Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later). Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II. Name and mailing address of the ISA/US Authorized offic Commissioner of Patents and Trademarks (ANE CARLSON, PH.D. KAREN COCH Box PCT Washington, D.C. 20231 (703) 308-0196 Telephone No. Facsimile No. (703) 305-3230

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING SUBMISSION OR TRANSMITTAL OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:	
MONACO, Daniel, A. Seidel, Gonda, Lavorgna E P.C. Suite 1800 Two Penn Center Plaza Philadelphia, PA 19102 ÉTATS-UNIS D'AMÉRIQU	DEC 2 1999
ETATO ONIO D'AIMENIAO	SEIDEL, GONDA, LAYORGNA, & MONACO, P.C.

Date of mailing (day/month/year) 08 December 1999 (08.12.99)	ETATS-UNIS D'AMÉRIQUE SEIDEL, GONDA, LAYORGNA, & MONACO, P.C.
Applicant's or agent's file reference 6056-279 PC	IMPORTANT NOTIFICATION
International application No. PCT/US99/22756	International filing date (day/month/year) 30 September 1999 (30.09.99)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 01 October 1998 (01.10.98)
Applicant	

- 1. The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- 2. This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- 3. An asterisk(*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- 4. The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

Priority date Priority application No. Country or regional Office or PCT receiving Office of priority document

01 Octo 1998 (01.10.98) 60/102,640 US 07 Dece 1999 (07.12.99)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Olivia RANAIVOJAONA

Facsimile No. (41-22) 740.14.35

FRONTICELLI, Clara

Telephone No. (41-22) 338.83.38

TENT CO JUL 1 7 2000 JUL 1 7 2000 SEIDEL, GONDA, LAVORGNA, & MONACO, P.C. INTERNATIONAL PRELIMINARY EXAMINING AUTH EIDEL, GONDA, LAVORGNA

To: DANIEL A. MONACO SEIDEL, GONDA, LAVORGNA, & MONACO, **SUITE 1800** TWO PENN CENTER PLAZA PHILADELPHIA PA 19102

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY **EXAMINATION REPORT**

(PCT Rule 71.1)

IMPORTANT NOTIFICATION

Date of Mailing (day/month/year) 2 JUL 2000

Applicant's or agent's file reference

6056-279 PC

International fiting date (day/month/year)

Priority Date (day/month/year)

PCT/US99/22756

International application No.

30 SEPTEMBER 1999

01 OCTOBER 1998

Applicant

From the

TEMPLE UNIVERSITY OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION

- Ι. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication 2. to all the elected Offices.
- 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

REMINDER 4.

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks Box PCT

Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

KAREN COCHRANE CARLSON, PH.D.

Telephone No. (703) 308-0196

Form PCT/IPEA/416 (July 1992) *

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 6056-279 PC			ransmittal of International Search Report as well as, where applicable, item 5 below.		
International application No.	International filing date (de	ty/month/year)	(Earliest) Priority Date (day/month/year)		
PCT/US99/22756	30 SEPTEMBER 1999	ļ	01 OCTOBER 1998		
Applicant FRONTICELLI, CLARA	••				
This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau. This international search report consists of a total of sheets. X It is also accompanied by a copy of each prior art document cited in this report.					
1. Certain claims were found	unsearchable (See Box I).				
2. Unity of invention is lacking	ng (See Box II).				
	contains disclosure of a nuited out on the basis of the sec		amino acid sequence listing and the		
	filed with the international ap-	plication.			
	furnished by the applicant sep	parately from the in	nternational application,		
	but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.				
	transcribed by this Authority.				
4. With regard to the title, X	the text is approved as submi	tted by the applica	ant.		
	the text has been established	by this Authority	to read as follows:		
5. With regard to the abstract,					
	the text is approved as submi	tted by the applica	ant.		
		ay, within one m	2 38.2(b), by this Authority as it appears north from the date of mailing of this this Authority.		
6. The figure of the drawings to be p	oublished with the abstract is:				
Figure No. 4	as suggested by the applicant		None of the figures.		
	because the applicant failed to	o suggest a figure.	~		
	because this figure better cha	racterizes the inve	ntion.		

INTERNATIONAL SEARCH REPORT

International application	No.
T/US99/22756	

A. CLASSIFICATION OF SUBJECT			
IPC(6) :C07K 14/805; C07H 17/00; C12P 21/06			
US CL: :530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/6 According to International Patent Classification (IPC) or to both national classification and IPC			
B. FIELDS SEARCHED			
Minimum documentation searched (classification)	ation system followed	by classification symbols)	
U.S. : 530/385; 536/23.1; 435/69.6, 320	-		
Documentation searched other than minimum	documentation to the	extent that such documents are included	in the fields searched
none			
Electronic data base consulted during the int	ternational search (na	me of data base and, where practicable,	, search terms used)
APS, Dialog			
C. DOCUMENTS CONSIDERED TO	BE RELEVANT		
Category* Citation of document, with	indication, where app	propriate, of the relevant passages	Relevant to claim No.
- · · · · · · · · · · · · · · · · · · ·	•	August 1996, see especially	23-24
_ · ·	nes 6-41; col. 1,	lines 44-45; col. 38, lines 1-	
Y 5.			1-22
		,	
Further documents are listed in the co	ontinuation of Box C	. See patent family annex.	<u> </u>
Special categories of cited documents:		"T" later document published after the int date and not in conflict with the app	
"A" document defining the general state of the ar to be of particular relevance	t which is not considered	the principle or theory underlying the	e invention
E earlier document published on or after the i	_	"X" document of particular relevance; the considered novel or cannot be considered	
"L" document which may throw doubts on prio cited to establish the publication date of a special reason (as specified)		"Y" document of particular relevance; the	
"O" document referring to an oral disclosure, means	use, exhibition or other	considered to involve an inventive combined with one or more other suc being obvious to a person skilled in	h documents, such combination
P document published prior to the internationa the priority date claimed	I filing date but later than	"&" document member of the same paten	
Date of the actual completion of the interna	tional search	Date of mailing of the international sec	arch report
18 JANUARY 2000		14,59	(U 00
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks		Authorized officer	Clin for
Box PCT Washington, D.C. 20231		KAREN COCHRANE CARLSON	, PH.D. A
Facsimile No. (703) 305-3230		Telephone No. (703) 308-0196	
Form PCT/ISA/210 (second sheet)(July 1992	2)*		

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 6056-279 PC	FOR FURTHER ACTION See Notification of Transmittal of Internationa Preliminary Examination Report (Form PCT/IPEA/416			
International application No.	International filing date (day/m	onth/year)	Priority date (day/month/year)	
PCT/US99/22756	99/22756 30 SEPTEMBER 1999 01 OCTOBER 1998			
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.				
Applicant TEMPLE UNIVERSITY OF THE CO	MMONWEALTH SYSTEM OF	HIGHER EDU	JCATION	
Examining Authority and is 2. This REPORT consists of a This report is also accombeen amended and are the (see Rule 70.16 and Sec	transmitted to the applicant a total of sheets. panied by ANNEXES, i.e., sheet basis for this report and/or she tion 607 of the Administrative I	s of the descrip	ntion, claims and/or drawings which have rectifications made before this Authority. der the PCT).	
These annexes consist of a to	otal of sheets.			
3. This report contains indications relating to the following items: I X Basis of the report				
Date of submission of the demand		of completion	of this report	
Name and mailing address of the IPEA Commissioner of Patents and Trade Box PCT Washington, D.C. 20231	marks K	AREN COCHI	Lelin for RANE CARLSON JPH.D.	
Facsimile No. (703) 305-3230		hone No. (7)	03) 308-0196	

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/22756

т. в	asis of the 1	report		
1. With	regard to the	elements of the intern	ational application:*	
x	_	tional application as		
	the descrip	- •		
х	pages			as originally filed
	pages	NONE		
	pages		, filed with the letter of	
	Pug03			
x	the claims:			
بننا	pages	27-30		, as originally filed
	pages	NONE	, as amended (together with ar	ny statement) under Article 19
	pages	NONE		, filed with the demand
	pages	NONE	, filed with the letter of	
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	the langua	ge of publication of	translated for the purposes of international search the international application (under Rule 48.3) mished for the purposes of international preliminary	b)).
	or 55.3).	e of the translation for	missied for the purposes of international preliminary	examination (thice) Rules 33.2 and
	•	-	or amino acid sequence disclosed in the internati ed out on the basis of the sequence listing:	onal application, the international
	contained	in the international	application in printed form.	
	filed toget	her with the interna	tional application in computer readable form.	
	furnished	subsequently to this	Authority in written form.	
	furnished	subsequently to this	Authority in computer readable form.	
	The statem internation	ent that the subseque al application as tiled	ently furnished written sequence listing does not and has been furnished.	go beyond the disclosure in the
	The statem been furnis		on recorded in computer readable form is identical to	o the writen sequence listing has
4. X	The amen	dments have resulte	ed in the cancellation of:	
1	X the	description, pages	NONE	
1		claims, Nos.		
		drawings, sheets/lig	· · · ·	
5. [~			than have been asset to a ter
'. L			(some of) the amendments had not been made, since	
in	placement she this report a	ets which have been fu	is indicated in the Supplemental Box (Rule 70.2(c)).* straished to the receiving Office in response to an invital and are not annexed to this report since they do not	tion under Article 14 are referred to
1	d 70.17). ny <u>replaceme</u> s	nt sheet containing su	uch ainendments must be referred to under item La	nd annexed to this report.



International application No.

PCT/US99/22756

	V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement				
statement					
Novelty (N)	Claims	1-24	YE		
	Claims	NONE	NO		
Inventive Step (IS)	Claims	1-24	YE		
	Claims	NONE	NC		
Industrial Auglioshilita (IA)	Claims	1-24	YE		
Industrial Applicability (IA)	Claims	NONE	NO		
	Cidinis				
delete cysteine residues in alpha or beta glo		 (USP 5,545,727) teach the latter, but do not teach of . 	or vaggest		
NEW CITATIONS					
NONE		• •			
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International application No.

PCT/US99/22756

Supplemental Box		
(To be used when the space	in any of the precedir	g boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

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The International Patent Classification (IPC) and/or the National classification are as listed below: IPC(7): C07K 14/805; C07H 17/00; C12P 21/06 and US Cl.: 530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/6





WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: C07K 14/805, C07H 17/00, C12P 21/06

A1

(11) International Publication Number:

WO 00/18802

(43) International Publication Date:

6 April 2000 (06.04.00)

(21) International Application Number:

PCT/US99/22756

(22) International Filing Date:

30 September 1999 (30.09.99)

(30) Priority Data:

60/102,640

1 October 1998 (\$\displaystyle{1}.10.98)

US

(71) Applicant (for all designated States except UNIVERSITY - OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION [US/US]; Broad Street and Montgomery Avenue, Philadelphia, PA 19122 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only):, FRONTICELLI, Clara [US/US]; 11514 Pebble Creek, Timonium, MD 21093 (US).

(74) Agent: MONACO, Daniel, A.; Seidel, Gonda, Lavorgna & Monaco, P.C., Suite 1800, Two Penn Center Plaza, Philadelphia, PA 19102 (US).

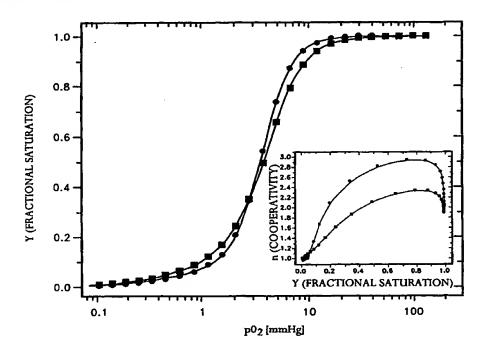
(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

With international search report.

Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: POLYMERIC HEMOGLOBIN MUTANTS



(57) Abstract

Human β -globin mutant polypeptides comprise the amino acid sequence of normal human β -globin modified by (i) the substitution or deletion of Cys at positions (93) and (112), and (ii) the substitution of a Cys for a non-Cys amino acid at one other position in the polypeptide, preferably Ser at position (9). Modified human hemoglobins containing this or other β -globin mutations, and/or an α -globin mutation, are provided, as well as polymers of such modified hemoglobins. Nucleic acids, vectors and transformed host cells for producing the β -globin mutants are provided.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΑZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Тодо
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DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/22756

A. CLASSIFICATION OF SUBJECT MATTER IPC(6) :C07K 14/805; C07H 17/00; C12P 21/06 US CL :530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/6 According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIELDS SEARCHED				
Minimum documentation searched (classification system follower	d by classification symbols)			
U.S. : 530/385; 536/23.1; 435/69.6, 320.1, 252.3; 325; 514/	6			
Documentation searched other than minimum documentation to the none	e extent that such documents are included in the fields searched			
Electronic data base consulted during the international search (na APS, Dialog	ame of data base and, where practicable, search terms used)			
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category* Citation of document, with indication, where ap	propriate, of the relevant passages Relevant to claim No.			
X US 5,545,727 A (HOFFMAN et al) 1:				
Example 28; col. 22, lines 6-41; col. 1	•			
Y 5.	1-22			
Further documents are listed in the continuation of Box C	See patent family annex.			
Special categories of cited documents:	"T" later document published after the international filing date or priority data and not in conflict with the application but cited to understand			
"A" document defining the general state of the art which is not considered to be of purticular relevance	the principle or theory underlying the invention			
"E" earlier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step			
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other	"Y" document of particular relevance; the claimed invention cannot be			
special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other	considered to involve an inventive step when the document is combined with one or more other such documents, such combination			
P document published prior to the international filing date but later than	being obvious to a person skilled in the art			
the priority date claimed	"&" document member of the same patent family			
Date of the actual completion of the international search 18 JANUARY 2000	Date of mailing of the international search report 14 FEB/2000			
Name and mailing address of the ISA/US	Authorized officer all a land			
Commissioner of Patents and Trademarks Box PCT	KAREN COCHRANE CARLSON, PH.D.			
Washington, D.C. 20231 Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196			

Form PCT/ISA/210 (second sheet)(July 1992)*

PAIENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT	То:
NOTIFICATION OF ELECTION (PCT Rule 61.2)	Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ETATS-UNIS D'AMERIQUE
Date of mailing (day/month/year) 16 May 2000 (16.05.00)	in its capacity as elected Office
International application No. PCT/US99/22756	Applicant's or agent's file reference 6056-279 PC
International filing date (day/month/year) 30 September 1999 (30.09.99)	Priority date (day/month/year) 01 October 1998 (01.10.98)
Applicant FRONTICELLI, Clara	
1. The designated Office is hereby notified of its election made: X In the demand filed with the International Preliminary Examining Authority on: 31 March 2000 (31.03.00) In a notice effecting later election filed with the International Bureau on:	
2. The election X was was not made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).	
The International Bureau of WIPO 34, chemin des Colombettes	Authorized officer Juan Cruz

Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

Facsimile No.: (41-22) 740.14.35

1211 Geneva 20, Switzerland